

**REMARKS**

Claims 50 to 72 are pending. Support for the new claims derive from the specification and claims as originally filed. Accordingly, the claims do not present new matter and entry is proper. Applicant reserves the right to claim additional subject matter and additional substitution positions in later cases.

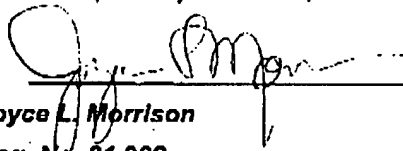
**Interview of May 24, 2005**

Applicant respectfully thanks the Examiner and his supervisor for their excellent advice from the interview. Applicant provided a background presentation of the mechanism of action of the TNF- $\alpha$  variants of the present invention. The claims were reviewed and it was agreed that applicant would delete from the claims the terms "naturally occurring" or "non-naturally occurring" or equivalent phrases from the claims. The Banner reference was discussed and it was pointed out that the focus of Banner was to identify receptor selective TNF- $\alpha$  variants to activate tumor killing functions without activating the deleterious effects associated with non-selective binding to the TNF receptors. Applicant's TNF- $\alpha$  variants (or variant homotrimers) are designed to exchange with endogenous TNF- $\alpha$  in a human to generate a mixed trimer composed of variant TNF- $\alpha$  proteins with the endogenous TNF monomers. These mixed trimers have reduced capacity to stimulate the signaling pathway associated with the endogenous TNF- $\alpha$  binding to the TNF receptors. Thus, while there are some overlapping of positions between Banner and the instant application, the purpose of the variants are different and would have a different result due to the lack of heterotrimers generated in Banner. Indeed, Banner never teaches or suggests the combination of variant TNF with native or endogenous TNF or the possibility that such a combination would lead to inactivation of native TNF.

Please direct further questions in connection with this Application to the undersigned at (626) 737-8019.

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Respectfully submitted,

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